

What is claimed is:

- 1 1. A polynucleotide that is regulated by a polypeptide comprising:
2 a regulatable, catalytically active polynucleotide, wherein the peptide interacts with
3 the polynucleotide to affect its catalytic activity.
- 1 2. The polynucleotide of claim 1, wherein the polypeptide is further defined as
2 being a protein.
- 1 3. The polynucleotide of claim 1, wherein the polypeptide comprises a peptide of
2 between about 7 and 20 amino acids.
- 1 4. The polynucleotide of claim 1, wherein the polypeptide comprises a peptide of
2 between about 7 and 12 amino acids.
- 1 5. The polynucleotide of claim 1, wherein the catalytic activity of the nucleic
2 acid is specific for a nucleic acid target sequence.
- 1 6. The polynucleotide of claim 1, wherein the catalytic activity of the nucleic
2 acid is regulated by the interaction of the nucleic acid with an effector.
- 1 7. The polynucleotide of claim 1, wherein the polynucleotide comprises RNA.
- 1 8. The polynucleotide of claim 1, wherein the polynucleotide comprises DNA
- 1 9. The polynucleotide of claim 1, wherein the polynucleotide is at least partially
2 single stranded.
- 1 10. The polynucleotide of claim 1, wherein the polynucleotide is at least partially
2 double stranded.
- 1 11. The polynucleotide of claim 1, wherein the polynucleotide comprises at least
2 one modified base.
- 1 12. The polynucleotide of claim 1, wherein the peptide is endogenous.
- 1 13. The polynucleotide of claim 1, wherein the peptide is exogenous.
- 1 14. The polynucleotide of claim 1, wherein the peptide comprises a
2 phosphorylated peptide.
- 1 15. A nucleic acid that is regulated by an effector comprising:
2 a regulatable, catalytically active nucleic acid, generated by the modification of at
3 least one catalytic residue.

1 16. The nucleic acid of claim 15, wherein the catalytic activity of the nucleic acid
2 is specific for a nucleic acid target sequence.

1 17. The nucleic acid of claim 15, wherein the catalytic activity of the nucleic acid
2 is regulated by the interaction of the nucleic acid with an effector.

1 18. The nucleic acid of claim 15, wherein the nucleic acid comprises RNA.

1 19. The nucleic acid of claim 15, wherein the nucleic acid comprises DNA.

1 20. The nucleic acid of claim 15, wherein the nucleic acid is at least partially
2 single stranded.

1 21. The nucleic acid of claim 15, wherein the nucleic acid is at least partially
2 double stranded.

1 22. The nucleic acid of claim 15, wherein the nucleic acid comprises at least one
2 modified base.

1 23. The nucleic acid of claim 15, wherein the effector is endogenous.

1 24. The nucleic acid of claim 15, wherein the effector is exogenous.

1 25. The nucleic acid of claim 15, wherein the effector comprises a protein.

1 26. The nucleic acid of claim 15, wherein the effector comprises a pharmaceutical
2 agent.

1 27. The nucleic acid of claim 15, wherein the effector comprises a protein
2 complex.

1 28. The nucleic acid of claim 15, wherein the effector comprises a peptide.

1 29. The nucleic acid of claim 15, wherein the effector a phosphorylated peptide.

1 30. The nucleic acid of claim 15, wherein the effector comprises a
2 dephosphorylated peptide.

1 31. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 causes the expression of a target gene to be up-regulated.

1 32. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 causes the expression of a target gene to be down-regulated.

1 33. The nucleic acid of claim 15, wherein the nucleic acid is used to detect at least
2 one exogenous effector from a library of candidate exogenous effector molecules.

1 34. The nucleic acid of claim 15, wherein the nucleic acid and the effector form a
2 nucleic acid-effector complex.

1 35. The nucleic acid of claim 15, wherein the nucleic acid and the effector is a
2 molecule that forms an nucleic acid-effector complex and the nucleic acid-effector complex
3 acts synergistically to affect the catalytic activity of the nucleic acid-effector complex.

1 36. The nucleic acid of claim 15, wherein the nucleic acid catalyses a ligation
2 reaction with an oligonucleotide substrate.

1 37. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 adds a non-oligonucleotide substrate.

1 38. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 adds biotin to the nucleic acid.

1 39. The nucleic acid of claim 15, wherein the nucleic acid catalyses a cleavage
2 reaction with an oligonucleotide substrate.

1 40. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of one or more effector-effectors that acts on the effector
3 molecule that interacts with the nucleic acid.

1 41. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of theophylline.

1 42. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure.

1 43. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure that comprises a virus
3 particle.

1 44. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure that comprises a cell wall.

1 45. A nucleic acid comprising:
2 a gene;
3 a regulatable, catalytically active nucleic acid inserted within the gene;
4 wherein the presence of an effector causes the nucleic acid to catalyze a reaction.

1 46. The nucleic acid of claim 45, wherein the catalytic reaction is a self-splicing
2 reaction.

1 47. The nucleic acid of claim 45, wherein the catalytic reaction is a ligation
2 reaction.

1 48. The nucleic acid of claim 45, wherein the catalytic reaction is a trans-cleavage
2 reaction.

1 49. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the gene.

1 50. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of one or more genes.

1 51. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the mRNA of the gene.

1 52. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the protein encoded by the gene.

1 53. A nucleic acid segment comprising:
2 a regulatable, catalytically active nucleic acid comprising one or more catalytic
3 nucleotides, selected from a pool of nucleic acids in which at least one of the catalytic
4 residues has been randomized.

1 54. A regulatable, catalytically active nucleic acid segment comprising:
2 an effector domain; and
3 a nucleic acid catalyst domain in which one or more catalytic residues of the nucleic
4 acid catalyst have been randomized;
5 wherein the kinetic parameters of the catalytic domain are regulated by an effector
6 that interacts with the effector domain.

1 55. A method of isolating a regulatable, catalytically active nucleic acid,
2 comprising the steps of:
3 randomizing at least one nucleotide in the catalytic domain of a catalytically active
4 nucleic acid to create a nucleic acid pool; and
5 removing from the nucleic acid pool those nucleic acids that interact with the
6 catalytic target of the catalytic domain.

1 56. The method of claim 55, further comprising the step of adding an effector to
2 the remaining pool of nucleic acids.

1 57. The method of claim 55, further comprising the steps of adding an effector to
2 the remaining nucleic acids, wherein the effector acts on the nucleic acids to alter the
3 catalytic activities of the nucleic acids.

1 58. The method of claim 55, further comprising the step of purifying the isolated
2 nucleic acid.

1 59. The method of claim 55, further comprising the step of sequencing the
2 isolated nucleic acid.

1 60. The method of claim 55, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 61. The method of claim 55, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 62. The method of claim 55, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 63. The method of claim 55, where the target is an mRNA molecule.

1 64. The method of claim 56, where the effector is a protein.

1 65. The method of claim 56, where the effector is a peptide.

1 66. The method of claim 56, where the effector is a phosphoprotein.

1 67. The method of claim 56, where the effector is a glycoprotein.

1 68. The method of claim 56, where the effector is light.

1 69. The method of claim 56, where the effector is visible light.

1 70. The method of claim 56, where the effector is a magnet.

1 71. The method of claim 55, where the target is a metabolic reaction.

1 72. The method of claim 55, in which nucleic acids with altered catalytic
2 specificity are selected in the presence of an effector.

1 73. The method of claim 55, in which nucleic acids with altered catalytic
2 activities are selected in the absence of an effector.

1 74. The method of claim 55, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of an effector.

1 75. The method of claim 55, the effector domain comprises a random sequence
2 pool.

1 76. The method of claim 55, the effector domain comprises a partially randomized
2 sequence pool.

1 77. A method of making a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector protein to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain.

1 78. A method of isolating a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 randomizing at least one nucleotide in the catalytic domain of a catalytically active
4 nucleic acid to create a nucleic acid pool;

5 removing from the nucleic acid pool those nucleic acids that interact with the
6 catalytic target of the catalytic domain;

7 adding an effector molecule to the nucleic acids; and

8 isolating those nucleic acids that interact with the catalytic target of the catalytic
9 domain.

1 79. A method of isolating a regulatable, catalytically active nucleic acid having a
2 catalytic and an effector domain, comprising the steps of:

3 randomizing at least one nucleotide in the catalytic domain of the nucleic acid to
4 create a nucleic acid pool;

5 removing from the nucleic acid pool those randomized nucleic acids that interact with
6 the catalytic target of the catalytic domain;

7 adding an effector to the nucleic acids; and

8 isolating the nucleic acids that interact with the catalytic target of the catalytic
9 domain.

1 80. An automated method of isolating a regulatable, catalytically active nucleic
2 acid having a catalytic and an effector domain, comprising the steps of:

3 (a) randomizing at least one nucleotide in the catalytic domain of the nucleic acid
4 to create a nucleic acid pool;

(b) removing from the nucleic acid pool those randomized nucleic acids that interact with the catalytic target of the catalytic domain;

(c) adding an effector to the nucleic acids;

(d) adding an effector-effector that specifically interacts with the effector; and

(e) isolating the nucleic acids that interact with the catalytic target of the catalytic domain; and

(f) repeating steps (a) through (e).

81. A method of detection of a target using a regulatable, catalytically active nucleic acid comprising the steps of:

contacting the a regulatable, catalytically active nucleic acid with the target; and

measuring the effect of the interaction between the a regulatable, catalytically active nucleic acid and the target.

82. A method of modifying a target using a regulatable, catalytically active nucleic acid comprising the steps of:

providing a regulatable, catalytically active nucleic acid capable of target specific modification; and

modifying the target under conditions that cause a regulatable, catalytically active nucleic acid-specific activity.

83. A biosensor comprising:

a solid support; and

at least one regulatable, catalytically active nucleic acid, wherein the kinetic parameters of the nucleic acid on a target vary in response to the interaction of an effector molecule with the nucleic acid;

wherein the at least one regulatable, catalytically active nucleic acid is immobilized on the support.

84. The biosensor of claim 83, wherein the reaction is machine readable.

85. The biosensor of claim 83, wherein the solid support comprises a multiwell plate.

86. The biosensor of claim 83, wherein the solid support comprises a surface plasmon resonance sensor.

1 87. The biosensor of claim 83, wherein the at least one regulatable, catalytically
2 active nucleic acids is covalently immobilized on the solid support.

1 88. The biosensor of claim 83, wherein the catalytic reaction produces a
2 detectable signal.

1 89. The biosensor of claim 83, wherein the catalytic reaction is the attachment of
2 a tag to the immobilized nucleic acids to produce the signal.

1 90. The biosensor of claim 83, wherein the substrate is further defined as
2 containing known nucleic acid sequences tags and the nucleic acids are sorted on the surface
3 of the substrate based on non-covalent hybridization to sequence tags.

1 91. A biosensor comprising:
2 a solid support; and
3 at least one regulatable, catalytically active nucleic acids, wherein the kinetic
4 parameters of the nucleic acids on a target vary in response to the interaction of an effector
5 molecule with the nucleic acid;

6 wherein catalytic targets of the catalytic domain is immobilized on the support.

1 92. A biosensor comprising:
2 a solid support; and
3 at least one regulatable, catalytically active nucleic acids, wherein the kinetic
4 parameters of the nucleic acids on a target vary in response to the interaction of an effector
5 molecule with the nucleic acid;

6 wherein the effector is immobilized on the support.

1 93. A method of selecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain;

11 introducing the nucleic acids into a host cell; and
12 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
13 the effector.

1 94. The method of claim 93, further comprising the step of purifying the isolated
2 nucleic acid.

1 95. The method of claim 93, further comprising the step of sequencing the
2 isolated nucleic acid.

1 96. The method of claim 93, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 97. The method of claim 93, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 98. The method of claim 93, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 99. The method of claim 93, where the target is an mRNA molecule.

1 100. The method of claim 93, where the effector is a protein.

1 101. The method of claim 93, where the effector is a peptide.

1 102. The method of claim 93, where the effector is a phosphoprotein.

1 103. The method of claim 93, where the effector is a glycoprotein.

1 104. The method of claim 93, where the effector is light.

1 105. The method of claim 93, where the effector is visible light.

1 106. The method of claim 93, where the effector is a magnet.

1 107. The method of claim 93, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of the effector.

1 108. The method of claim 93, the effector domain comprises a completely random
2 sequence pool.

1 109. The method of claim 93, the effector domain comprises a partially randomized
2 sequence pool.

1 110. A method of selecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain;

11 introducing the nucleic acids into a host cell; and

12 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
13 the effector.

1 111. The method of claim 110, further comprising the step of purifying the isolated
2 nucleic acid.

1 112. The method of claim 110, further comprising the step of sequencing the
2 isolated nucleic acid.

1 113. The method of claim 110, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 114. The method of claim 110, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 115. The method of claim 110, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 116. The method of claim 110, where the target is an mRNA molecule.

1 117. The method of claim 110, where the effector is a protein.

1 118. The method of claim 110, where the effector is a peptide.

1 119. The method of claim 110, where the effector is a phosphoprotein.

1 120. The method of claim 110, where the effector is a glycoprotein.

1 121. The method of claim 110, where the effector is light.

1 122. The method of claim 110, where the effector is visible light.

1 123. The method of claim 110, where the effector is a magnet.

1 124. The method of claim 110, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of the effector.

1 125. The method of claim 110, the effector domain comprises a completely random
2 sequence pool.

1 126. The method of claim 110, the effector domain comprises a partially
2 randomized nucleotide sequence.

1 127. A method of detecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 isolating a regulatable, catalytically active nucleic acid;

4 creating a construct in which the nucleic acid is in position to regulate the expression
5 of a reporter gene;

6 introducing the construct into a host cell; and

7 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
8 an effector.

1 128. A vector comprising:

2 a regulatable, catalytically active polynucleotide, wherein the peptide molecule
3 interacts with the polynucleotide to affect its catalytic activity.

1 129. A vector comprising:

2 a regulatable, catalytically active nucleic acid, generated by the modification of at
3 least one catalytic residue.

1 130. A method of modulating expression of a nucleic acid, the method comprising
2 providing a polynucleotide that is regulated by a peptide, the polynucleotide
3 comprising a regulatable, catalytically active polynucleotide, wherein the peptide interacts
4 with the polynucleotide to affect its catalytic activity; and

5 contacting the polynucleotide with the peptide, thereby modulating expression of a
6 nucleic acid.

1 131. The method of claim 130, wherein the polynucleotide is provided in a cell.

1 132. The method of claim 131, wherein the cell is provided in vitro.

1 133. The method of claim 131, wherein the cell is provided in vivo.

1 134. The method of claim 131, wherein the cell is a prokaryotic cell.

1 135. The method of claim 131, wherein the cell is a eukaryotic cell.

1 136. A method of modulating expression of a nucleic acid, the method comprising
2 the steps of:

- 3 providing a nucleic acid that is regulated by an effector, the nucleic acid comprising:
4 a regulatable, catalytically active nucleic acid, wherein the regulatable, catalytically active
5 nucleic acid molecule includes at least one modified catalytic residue; and
6 contacting the nucleic acid with the effector, thereby modulating expression of a
7 nucleic acid.